Clinical trial results:
A Phase III, Open-label Extension Trial of ECU-MG-301 to Evaluate the Safety and Efficacy of Eculizumab in Subjects with Refractory Generalized Myasthenia Gravis (gMG)

Summary

EudraCT number	2013-002191-41
Trial protocol	GB IT BE DE SE HU ES NL DK CZ FI
Global end of trial date	15 January 2019

Results information

Result version number	v1
This version publication date	27 December 2019
First version publication date	27 December 2019

Trial information

Trial identification

Sponsor protocol code	ECU-MG-302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02301624
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Alexion Pharmaceuticals, Inc.
Sponsor organisation address	121 Seaport Blvd, Boston, MA, United States, 02210
Public contact	European Clinical Trial Information, Alexion Europe SAS, +33 147100615, clinicaltrials.eu@alexion.com
Scientific contact	European Clinical Trial Information, Alexion Europe SAS, +33 147100615, clinicaltrials.eu@alexion.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 January 2019
Global end of trial reached?	Yes
Global end of trial date	15 January 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and efficacy of eculizumab in the treatment of refractory generalized myasthenia gravis (gMG) as an extension study for the participants who completed Study ECU-MG-301 (2013-003589-15).

Protection of trial subjects:

This study was conducted in accordance with the International Council on Harmonisation (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which the study was conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 November 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Czech Republic: 3
Country: Number of subjects enrolled	Denmark: 6
Country: Number of subjects enrolled	Finland: 1
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Argentina: 6
Country: Number of subjects enrolled	Brazil: 6
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Japan: 11
Country: Number of subjects enrolled	Korea, Republic of: 5
Country: Number of subjects enrolled	Turkey: 5
Country: Number of subjects enrolled	United States: 41
Worldwide total number of subjects	117
EEA total number of subjects	41

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	97
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

After receiving blinded study treatment (eculizumab or placebo) in Study ECU-MG-301 (2013-003589-15) for 26 weeks, participants were eligible to enroll in the ECU-MG-302 extension study. Participants were to enter Study ECU-MG-302 within 2 weeks after completing their Week 26 visit in Study ECU-MG-301.

Period 1

Period 1 title	Blind Induction Phase
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

Study ECU-MG-302 had a 4-week Blind Induction Phase that was specifically designed to maintain each participant's blinded treatment assignment in Study ECU MG 301. As a result, all assessments performed during the first 4 weeks of Study ECU-MG-302 were conducted under blinded conditions.

Arms

Are arms mutually exclusive?	Yes
Arm title	Blind Induction: Eculizumab/Eculizumab

Arm description:

Blind Induction Phase: Participants who had received blinded treatment with eculizumab in Study ECU-MG-301 were administered eculizumab (4 vials/1200 mg) on Day 1 and Week 2 and placebo (4 vials/0 mg) at Weeks 1 and 3.

Arm type	Experimental
Investigational medicinal product name	Eculizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Eculizumab was packed in a single 30 milliliter (mL) vial as a solution with a concentration of 10 mg/mL, with a unit dose of 300 mg in an intravenous infusion.

Investigational medicinal product name	Blind Induction: Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

A clear, colorless solution in an identical 30 mL vial without the active ingredient.

Arm title	Blind Induction: Placebo/Eculizumab

Arm description:

Blind Induction Phase: Participants who had received blinded treatment with placebo in Study ECU-MG-301 were administered eculizumab/placebo (3 vials/900 mg, plus 1 vial/0 mg, respectively) on Day 1 and Weeks 1 through 3.

Arm type	Experimental
Investigational medicinal product name	Eculizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Eculizumab was packed in a single 30-mL vial as a solution with a concentration of 10 mg/mL, with a unit dose of 300 mg in an intravenous infusion.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

A clear, colorless solution in an identical 30 mL vial without the active ingredient.

Number of subjects in period 1	Blind Induction: Eculizumab/Eculizumab	Blind Induction: Placebo/Eculizumab
Started	56	61
Received at least 1 dose of study drug	56	61
Completed	55	61
Not completed	1	0
Consent withdrawn by subject	1	-

Period 2

Period 2 title	Open-label Maintenance Phase
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Open-label: Eculizumab/Eculizumab

Arm description:

Open-Label Maintenance Phase: Participants received open-label eculizumab (4 vials/1200 mg) every 2 weeks starting at Week 4 and continued throughout the study. Eculizumab 1200 mg was administered for up to 4 years in this extension study.
Participants had previously received blinded treatment with eculizumab in Study ECU-MG-301.

Arm type	Experimental
Investigational medicinal product name	Eculizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

All participants received eculizumab 1200 mg every 2 weeks during the Open-Label Maintenance Phase. Eculizumab was packed in a single 30 milliliter (mL) vial as a solution with a concentration of 10 mg/mL, with a unit dose of 300 mg in an intravenous infusion.

Arm title	Open-label: Placebo/Eculizumab

Arm description:

Open-Label Maintenance Phase: Participants received open-label eculizumab (4 vials/1200 mg) every 2 weeks starting at Week 4 and continued throughout the study. Eculizumab 1200 mg was administered for up to 4 years in this extension study.
Participants had previously received blinded treatment with placebo in Study ECU-MG-301.

Arm type	Experimental
Investigational medicinal product name	Eculizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

All participants received eculizumab 1200 mg every 2 weeks during the Open-Label Maintenance Phase. Eculizumab was packed in a single 30-mL vial as a solution with a concentration of 10 mg/mL, with a unit dose of 300 mg in an intravenous infusion.

Number of subjects in period 2	Open-label: Eculizumab/Eculizumab	Open-label: Placebo/Eculizumab
Started	55	61
Received at least 1 dose of study drug	55	61
Completed	43	44
Not completed	12	17
Physician decision	3	3
Consent withdrawn by subject	4	8
Adverse event, non-fatal	2	5
Death	2	1
Participant felt no change in condition	1	-

Baseline characteristics

Reporting groups

Reporting group title	Blind Induction: Eculizumab/Eculizumab

Reporting group description:

Blind Induction Phase: Participants who had received blinded treatment with eculizumab in Study ECU-MG-301 were administered eculizumab (4 vials/1200 mg) on Day 1 and Week 2 and placebo (4 vials/0 mg) at Weeks 1 and 3.

Reporting group title	Blind Induction: Placebo/Eculizumab

Reporting group description:

Blind Induction Phase: Participants who had received blinded treatment with placebo in Study ECU-MG-301 were administered eculizumab/placebo (3 vials/900 mg, plus 1 vial/0 mg, respectively) on Day 1 and Weeks 1 through 3.

Reporting group values	Blind Induction: Eculizumab/Eculizumab	Blind Induction: Placebo/Eculizumab	Total
Number of subjects	56	61	117
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	47	50	97
From 65-84 years	9	11	20
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	47.2	47.5	
standard deviation	± 15.52	± 17.85	-
Gender categorical Units: Subjects			
Female	38	41	79
Male	18	20	38
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	8	10	18
Not Hispanic or Latino	45	48	93
Unknown or Not Reported	3	3	6
Race/Ethnicity, Customized Units: Subjects			
Asian	3	16	19
Black or African American	0	2	2
White	47	41	88

Multiple	1	0	1
Unknown	1	0	1
Other	4	2	6

End points

End points reporting groups

Reporting group title	Blind Induction: Eculizumab/Eculizumab

Reporting group description:

Blind Induction Phase: Participants who had received blinded treatment with eculizumab in Study ECU-MG-301 were administered eculizumab (4 vials/1200 mg) on Day 1 and Week 2 and placebo (4 vials/0 mg) at Weeks 1 and 3.

Reporting group title	Blind Induction: Placebo/Eculizumab

Reporting group description:

Blind Induction Phase: Participants who had received blinded treatment with placebo in Study ECU-MG-301 were administered eculizumab/placebo (3 vials/900 mg, plus 1 vial/0 mg, respectively) on Day 1 and Weeks 1 through 3.

Reporting group title	Open-label: Eculizumab/Eculizumab

Reporting group description:

Open-Label Maintenance Phase: Participants received open-label eculizumab (4 vials/1200 mg) every 2 weeks starting at Week 4 and continued throughout the study. Eculizumab 1200 mg was administered for up to 4 years in this extension study.
Participants had previously received blinded treatment with eculizumab in Study ECU-MG-301.

Reporting group title	Open-label: Placebo/Eculizumab

Reporting group description:

Open-Label Maintenance Phase: Participants received open-label eculizumab (4 vials/1200 mg) every 2 weeks starting at Week 4 and continued throughout the study. Eculizumab 1200 mg was administered for up to 4 years in this extension study.
Participants had previously received blinded treatment with placebo in Study ECU-MG-301.

Subject analysis set title	Eculizumab/Eculizumab
Subject analysis set type	Full analysis

Subject analysis set description:

Blind Induction Phase: Participants who had received blinded treatment with eculizumab in Study ECU-MG-301 were administered eculizumab (4 vials/1200 mg) on Day 1 and Week 2 and placebo (4 vials/0 mg) at Weeks 1 and 3.
Open-Label Maintenance Phase: Participants received open-label eculizumab (4 vials/1200 mg) every 2 weeks starting at Week 4 and continued throughout the study.
Eculizumab 1200 mg was administered for up to 4 years in this extension study.

Subject analysis set title	Placebo/Eculizumab
Subject analysis set type	Full analysis

Subject analysis set description:

Blind Induction Phase: Participants who had received blinded treatment with placebo in Study ECU-MG-301 were administered eculizumab/placebo (3 vials/900 mg, plus 1 vial/0 mg, respectively) on Day 1 and Weeks 1 through 3.
Open-Label Maintenance Phase: Participants received open-label eculizumab (4 vials/1200 mg) every 2 weeks starting at Week 4 and continued throughout the study.
Eculizumab 1200 mg was administered for up to 4 years in this extension study

Primary: Number Of Participants With Treatment-Emergent Adverse Events

End point title	Number Of Participants With Treatment-Emergent Adverse Events[1]

End point description:

Treatment-emergent adverse events (TEAEs) are adverse events with onset on or after the first study drug dose in Study ECU-MG-302. Likewise, treatment-emergent serious adverse events (TESAEs) are serious adverse events that onset on or after the first study drug dose in Study ECU-MG-302. A summary of serious and all other non-serious adverse events, regardless of causality, is located in the Adverse events section.

End point type	Primary

End point timeframe:

Day 1 (after dosing) through End of Study (Week 208)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were planned.

End point values	Eculizumab/Eculizumab	Placebo/Eculizumab		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	56	61		
Units: Participants				
TEAEs	55	59		
TEAEs leading to withdrawal	3	5		
TESAEs	30	30		
TESAEs leading to withdrawal	3	4		
Deaths	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline In Myasthenia Gravis Activities Of Daily Living Profile (MG-ADL) Total Score At Last Assessment

End point title	Change From Baseline In Myasthenia Gravis Activities Of Daily Living Profile (MG-ADL) Total Score At Last Assessment

End point description:

The MG-ADL scale is a validated 8-item patient-reported outcome measure. Participants assessed their functional disability secondary to ocular (2 items), bulbar (3 items), respiratory (1 item), and gross motor or limb impairment (2 items). These 8 items were not weighted and were individually graded from 0 (normal) to 3 (most severe), providing a total MG-ADL score ranging from 0 to 24 points. A reduction in score indicates improvement in condition. The ECU-MG-302 Baseline was defined as the last available assessment prior to treatment (first study drug infusion) with eculizumab in ECU-MG-302. ECU-MG-301 Baseline was defined as the last available assessment prior to treatment (first study drug infusion). Last assessment was the last available assessment of a participant up to the end of treatment in the study.

End point type	Secondary

End point timeframe:

Baseline, Last Assessment

End point values	Eculizumab/Eculizumab	Placebo/Eculizumab		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	56	61		
Units: Units on a scale				
arithmetic mean (standard deviation)				
ECU-MG-302 Baseline	5.8 (± 4.27)	7.6 (± 3.63)		
Change from ECU-MG-302 Baseline	-0.00 (± 3.97)	-2.7 (± 4.15)		
ECU-MG-301 Baseline	10.3 (± 3.03)	9.9 (± 2.58)		

Change from ECU-MG-301 Baseline	-4.5 (± 3.96)	-5.0 (± 3.39)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 1 after dosing of study drug through Week 208.	
Adverse event reporting additional description:	
All eligible-enrolled participants who received at least 1 dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	Eculizumab/Eculizumab
Reporting group description:	
All participants who received at least 1 dose of study drug in this extension study. Participants had previously received blinded treatment with eculizumab in Study ECU-MG-301.	
Reporting group title	Placebo/Eculizumab
Reporting group description:	
All participants who received at least 1 dose of study drug in this extension study. Participants had previously received blinded treatment with placebo in Study ECU-MG-301.	
Reporting group title	Eculizumab (Combined Total)
Reporting group description:	
All participants who received at least 1 dose of eculizumab in the extension study. Participants received open-label eculizumab (4 vials/1200 mg) every 2 weeks starting at Week 4 and continued throughout the study. Eculizumab 1200 mg was administered for up to 4 years in this extension study.	

Serious adverse events	Eculizumab/Eculizumab	Placebo/Eculizumab	Eculizumab (Combined Total)
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 56 (53.57%)	30 / 61 (49.18%)	60 / 117 (51.28%)
number of deaths (all causes)	2	1	3
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	1 / 56 (1.79%)	1 / 61 (1.64%)	2 / 117 (1.71%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoma			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma in situ			

subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuroendocrine carcinoma			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed[1]	0 / 18 (0.00%)	1 / 20 (5.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin papilloma			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arterial occlusive disease			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extremity necrosis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lupus vasculitis			

subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	3 / 56 (5.36%)	0 / 61 (0.00%)	3 / 117 (2.56%)
occurrences causally related to treatment / all	2 / 3	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Autoimmune disorder			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed[2]	0 / 38 (0.00%)	1 / 41 (2.44%)	1 / 79 (1.27%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed[3]	1 / 38 (2.63%)	0 / 41 (0.00%)	1 / 79 (1.27%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal haemorrhage			

subjects affected / exposed[4]	1 / 38 (2.63%)	0 / 41 (0.00%)	1 / 79 (1.27%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 56 (0.00%)	3 / 61 (4.92%)	3 / 117 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 56 (0.00%)	2 / 61 (3.28%)	2 / 117 (1.71%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary congestion			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 56 (0.00%)	3 / 61 (4.92%)	3 / 117 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Respiratory distress			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			

Depression			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Haemoglobin decreased			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula fracture			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrostomy tube site complication			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	2 / 56 (3.57%)	0 / 61 (0.00%)	2 / 117 (1.71%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pain			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Rib fracture			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve incompetence			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiogenic shock			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Encephalopathy			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 56 (1.79%)	2 / 61 (3.28%)	3 / 117 (2.56%)
occurrences causally related to treatment / all	1 / 1	1 / 2	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myasthenia gravis			
subjects affected / exposed	7 / 56 (12.50%)	9 / 61 (14.75%)	16 / 117 (13.68%)
occurrences causally related to treatment / all	2 / 13	3 / 16	6 / 29
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myasthenia gravis crisis			
subjects affected / exposed	2 / 56 (3.57%)	2 / 61 (3.28%)	4 / 117 (3.42%)
occurrences causally related to treatment / all	0 / 2	1 / 2	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Quadriparesis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	2 / 56 (3.57%)	1 / 61 (1.64%)	3 / 117 (2.56%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Histiocytosis haematophagic			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal incarcerated hernia			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspepsia			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Chronic hepatic failure			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Hepatic failure			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	1 / 56 (1.79%)	1 / 61 (1.64%)	2 / 117 (1.71%)
occurrences causally related to treatment / all	1 / 1	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis reactive			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot deformity			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture nonunion			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Myositis			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovitis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspergillus infection			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asymptomatic bacteriuria			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 56 (1.79%)	1 / 61 (1.64%)	2 / 117 (1.71%)
occurrences causally related to treatment / all	2 / 2	0 / 1	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis infective staphylococcal			

subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonic abscess			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related sepsis			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 56 (1.79%)	2 / 61 (3.28%)	3 / 117 (2.56%)
occurrences causally related to treatment / all	1 / 1	2 / 2	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	2 / 56 (3.57%)	0 / 61 (0.00%)	2 / 117 (1.71%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised infection			
subjects affected / exposed	1 / 56 (1.79%)	1 / 61 (1.64%)	2 / 117 (1.71%)
occurrences causally related to treatment / all	1 / 1	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis meningococcal			

subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital cellulitis			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 56 (3.57%)	2 / 61 (3.28%)	4 / 117 (3.42%)
occurrences causally related to treatment / all	1 / 2	1 / 3	2 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonal sepsis			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonas infection			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal abscess			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	2 / 56 (3.57%)	1 / 61 (1.64%)	3 / 117 (2.56%)
occurrences causally related to treatment / all	2 / 2	0 / 1	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			

subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 56 (1.79%)	1 / 61 (1.64%)	2 / 117 (1.71%)
occurrences causally related to treatment / all	1 / 1	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 56 (0.00%)	2 / 61 (3.28%)	2 / 117 (1.71%)
occurrences causally related to treatment / all	0 / 0	2 / 3	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Central obesity			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 56 (0.00%)	1 / 61 (1.64%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obesity			
subjects affected / exposed	1 / 56 (1.79%)	0 / 61 (0.00%)	1 / 117 (0.85%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Adverse event affected male participants only.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Adverse event affected female participants only.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Adverse event affected female participants only.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Adverse event affected female participants only.

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Eculizumab/Eculizumab	Placebo/Eculizumab	Eculizumab (Combined Total)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 56 (96.43%)	59 / 61 (96.72%)	113 / 117 (96.58%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma			
subjects affected / exposed	2 / 56 (3.57%)	4 / 61 (6.56%)	6 / 117 (5.13%)
occurrences (all)	2	19	21
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 56 (10.71%)	0 / 61 (0.00%)	6 / 117 (5.13%)
occurrences (all)	8	0	8
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 56 (14.29%)	7 / 61 (11.48%)	15 / 117 (12.82%)
occurrences (all)	9	7	16
Pyrexia			
subjects affected / exposed	5 / 56 (8.93%)	8 / 61 (13.11%)	13 / 117 (11.11%)
occurrences (all)	5	14	19
Influenza like illness			
subjects affected / exposed	4 / 56 (7.14%)	3 / 61 (4.92%)	7 / 117 (5.98%)
occurrences (all)	4	7	11
Oedema peripheral			
subjects affected / exposed	4 / 56 (7.14%)	3 / 61 (4.92%)	7 / 117 (5.98%)
occurrences (all)	6	4	10
Chest pain			
subjects affected / exposed	4 / 56 (7.14%)	2 / 61 (3.28%)	6 / 117 (5.13%)
occurrences (all)	5	2	7

Peripheral swelling			
subjects affected / exposed	3 / 56 (5.36%)	2 / 61 (3.28%)	5 / 117 (4.27%)
occurrences (all)	3	2	5
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	3 / 56 (5.36%)	7 / 61 (11.48%)	10 / 117 (8.55%)
occurrences (all)	4	8	12
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed[5]	3 / 38 (7.89%)	0 / 41 (0.00%)	3 / 79 (3.80%)
occurrences (all)	4	0	4
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	12 / 56 (21.43%)	10 / 61 (16.39%)	22 / 117 (18.80%)
occurrences (all)	15	13	28
Oropharyngeal pain			
subjects affected / exposed	3 / 56 (5.36%)	9 / 61 (14.75%)	12 / 117 (10.26%)
occurrences (all)	4	11	15
Asthma			
subjects affected / exposed	3 / 56 (5.36%)	2 / 61 (3.28%)	5 / 117 (4.27%)
occurrences (all)	6	2	8
Productive cough			
subjects affected / exposed	3 / 56 (5.36%)	1 / 61 (1.64%)	4 / 117 (3.42%)
occurrences (all)	4	4	8
Psychiatric disorders			
Depression			
subjects affected / exposed	3 / 56 (5.36%)	8 / 61 (13.11%)	11 / 117 (9.40%)
occurrences (all)	3	10	13
Insomnia			
subjects affected / exposed	7 / 56 (12.50%)	2 / 61 (3.28%)	9 / 117 (7.69%)
occurrences (all)	7	2	9
Anxiety			
subjects affected / exposed	4 / 56 (7.14%)	4 / 61 (6.56%)	8 / 117 (6.84%)
occurrences (all)	5	4	9
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	8 / 56 (14.29%)	6 / 61 (9.84%)	14 / 117 (11.97%)
occurrences (all)	16	11	27
Contusion			
subjects affected / exposed	7 / 56 (12.50%)	5 / 61 (8.20%)	12 / 117 (10.26%)
occurrences (all)	15	8	23
Infusion related reaction			
subjects affected / exposed	4 / 56 (7.14%)	7 / 61 (11.48%)	11 / 117 (9.40%)
occurrences (all)	9	31	40
Procedural pain			
subjects affected / exposed	2 / 56 (3.57%)	4 / 61 (6.56%)	6 / 117 (5.13%)
occurrences (all)	5	4	9
Ligament sprain			
subjects affected / exposed	3 / 56 (5.36%)	2 / 61 (3.28%)	5 / 117 (4.27%)
occurrences (all)	4	2	6
Tooth fracture			
subjects affected / exposed	3 / 56 (5.36%)	1 / 61 (1.64%)	4 / 117 (3.42%)
occurrences (all)	3	1	4
Rib fracture			
subjects affected / exposed	3 / 56 (5.36%)	0 / 61 (0.00%)	3 / 117 (2.56%)
occurrences (all)	3	0	3
Cardiac disorders			
Tachycardia			
subjects affected / exposed	4 / 56 (7.14%)	2 / 61 (3.28%)	6 / 117 (5.13%)
occurrences (all)	4	5	9
Atrial fibrillation			
subjects affected / exposed	4 / 56 (7.14%)	1 / 61 (1.64%)	5 / 117 (4.27%)
occurrences (all)	5	1	6
Palpitations			
subjects affected / exposed	1 / 56 (1.79%)	4 / 61 (6.56%)	5 / 117 (4.27%)
occurrences (all)	1	4	5
Nervous system disorders			
Headache			
subjects affected / exposed	20 / 56 (35.71%)	24 / 61 (39.34%)	44 / 117 (37.61%)
occurrences (all)	31	41	72
Myasthenia gravis			

subjects affected / exposed	12 / 56 (21.43%)	5 / 61 (8.20%)	17 / 117 (14.53%)
occurrences (all)	15	5	20
Dizziness			
subjects affected / exposed	3 / 56 (5.36%)	6 / 61 (9.84%)	9 / 117 (7.69%)
occurrences (all)	7	7	14
Migraine			
subjects affected / exposed	4 / 56 (7.14%)	3 / 61 (4.92%)	7 / 117 (5.98%)
occurrences (all)	4	3	7
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 56 (8.93%)	3 / 61 (4.92%)	8 / 117 (6.84%)
occurrences (all)	6	3	9
Iron deficiency anaemia			
subjects affected / exposed	3 / 56 (5.36%)	2 / 61 (3.28%)	5 / 117 (4.27%)
occurrences (all)	3	2	5
Lymphopenia			
subjects affected / exposed	3 / 56 (5.36%)	0 / 61 (0.00%)	3 / 117 (2.56%)
occurrences (all)	3	0	3
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	3 / 56 (5.36%)	4 / 61 (6.56%)	7 / 117 (5.98%)
occurrences (all)	4	5	9
Ear pain			
subjects affected / exposed	2 / 56 (3.57%)	4 / 61 (6.56%)	6 / 117 (5.13%)
occurrences (all)	3	4	7
Eye disorders			
Cataract			
subjects affected / exposed	4 / 56 (7.14%)	5 / 61 (8.20%)	9 / 117 (7.69%)
occurrences (all)	5	5	10
Dry eye			
subjects affected / exposed	2 / 56 (3.57%)	4 / 61 (6.56%)	6 / 117 (5.13%)
occurrences (all)	2	4	6
Eye pain			
subjects affected / exposed	0 / 56 (0.00%)	4 / 61 (6.56%)	4 / 117 (3.42%)
occurrences (all)	0	4	4
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	15 / 56 (26.79%)	14 / 61 (22.95%)	29 / 117 (24.79%)
occurrences (all)	20	23	43
Nausea			
subjects affected / exposed	9 / 56 (16.07%)	13 / 61 (21.31%)	22 / 117 (18.80%)
occurrences (all)	13	14	27
Abdominal discomfort			
subjects affected / exposed	4 / 56 (7.14%)	6 / 61 (9.84%)	10 / 117 (8.55%)
occurrences (all)	4	6	10
Vomiting			
subjects affected / exposed	3 / 56 (5.36%)	7 / 61 (11.48%)	10 / 117 (8.55%)
occurrences (all)	3	10	13
Abdominal pain upper			
subjects affected / exposed	2 / 56 (3.57%)	6 / 61 (9.84%)	8 / 117 (6.84%)
occurrences (all)	2	6	8
Toothache			
subjects affected / exposed	3 / 56 (5.36%)	5 / 61 (8.20%)	8 / 117 (6.84%)
occurrences (all)	5	6	11
Dental caries			
subjects affected / exposed	2 / 56 (3.57%)	5 / 61 (8.20%)	7 / 117 (5.98%)
occurrences (all)	3	5	8
Dyspepsia			
subjects affected / exposed	2 / 56 (3.57%)	4 / 61 (6.56%)	6 / 117 (5.13%)
occurrences (all)	2	5	7
Abdominal pain			
subjects affected / exposed	3 / 56 (5.36%)	2 / 61 (3.28%)	5 / 117 (4.27%)
occurrences (all)	3	3	6
Tooth disorder			
subjects affected / exposed	3 / 56 (5.36%)	0 / 61 (0.00%)	3 / 117 (2.56%)
occurrences (all)	3	0	3
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	4 / 56 (7.14%)	4 / 61 (6.56%)	8 / 117 (6.84%)
occurrences (all)	4	4	8
Eczema			

subjects affected / exposed	3 / 56 (5.36%)	3 / 61 (4.92%)	6 / 117 (5.13%)
occurrences (all)	3	3	6
Rash			
subjects affected / exposed	3 / 56 (5.36%)	3 / 61 (4.92%)	6 / 117 (5.13%)
occurrences (all)	4	5	9
Alopecia			
subjects affected / exposed	3 / 56 (5.36%)	2 / 61 (3.28%)	5 / 117 (4.27%)
occurrences (all)	3	2	5
Urticaria			
subjects affected / exposed	3 / 56 (5.36%)	1 / 61 (1.64%)	4 / 117 (3.42%)
occurrences (all)	3	1	4
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	3 / 56 (5.36%)	1 / 61 (1.64%)	4 / 117 (3.42%)
occurrences (all)	3	1	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	11 / 56 (19.64%)	12 / 61 (19.67%)	23 / 117 (19.66%)
occurrences (all)	18	13	31
Pain in extremity			
subjects affected / exposed	9 / 56 (16.07%)	8 / 61 (13.11%)	17 / 117 (14.53%)
occurrences (all)	12	9	21
Back pain			
subjects affected / exposed	5 / 56 (8.93%)	7 / 61 (11.48%)	12 / 117 (10.26%)
occurrences (all)	7	11	18
Muscle spasms			
subjects affected / exposed	5 / 56 (8.93%)	6 / 61 (9.84%)	11 / 117 (9.40%)
occurrences (all)	7	6	13
Neck pain			
subjects affected / exposed	5 / 56 (8.93%)	4 / 61 (6.56%)	9 / 117 (7.69%)
occurrences (all)	5	4	9
Musculoskeletal pain			
subjects affected / exposed	3 / 56 (5.36%)	4 / 61 (6.56%)	7 / 117 (5.98%)
occurrences (all)	3	4	7
Myalgia			

subjects affected / exposed	5 / 56 (8.93%)	7 / 61 (11.48%)	12 / 117 (10.26%)
occurrences (all)	8	19	27
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	20 / 56 (35.71%)	22 / 61 (36.07%)	42 / 117 (35.90%)
occurrences (all)	36	49	85
Upper respiratory tract infection			
subjects affected / exposed	12 / 56 (21.43%)	15 / 61 (24.59%)	27 / 117 (23.08%)
occurrences (all)	34	28	62
Influenza			
subjects affected / exposed	11 / 56 (19.64%)	10 / 61 (16.39%)	21 / 117 (17.95%)
occurrences (all)	15	14	29
Urinary tract infection			
subjects affected / exposed	10 / 56 (17.86%)	8 / 61 (13.11%)	18 / 117 (15.38%)
occurrences (all)	13	18	31
Bronchitis			
subjects affected / exposed	6 / 56 (10.71%)	7 / 61 (11.48%)	13 / 117 (11.11%)
occurrences (all)	15	7	22
Gastroenteritis			
subjects affected / exposed	6 / 56 (10.71%)	5 / 61 (8.20%)	11 / 117 (9.40%)
occurrences (all)	7	6	13
Sinusitis			
subjects affected / exposed	7 / 56 (12.50%)	4 / 61 (6.56%)	11 / 117 (9.40%)
occurrences (all)	20	4	24
Gastroenteritis viral			
subjects affected / exposed	4 / 56 (7.14%)	6 / 61 (9.84%)	10 / 117 (8.55%)
occurrences (all)	4	9	13
Pneumonia			
subjects affected / exposed	4 / 56 (7.14%)	6 / 61 (9.84%)	10 / 117 (8.55%)
occurrences (all)	4	8	12
Cellulitis			
subjects affected / exposed	4 / 56 (7.14%)	4 / 61 (6.56%)	8 / 117 (6.84%)
occurrences (all)	6	5	11
Oral herpes			
subjects affected / exposed	3 / 56 (5.36%)	3 / 61 (4.92%)	6 / 117 (5.13%)
occurrences (all)	6	4	10

Tonsillitis			
subjects affected / exposed	1 / 56 (1.79%)	4 / 61 (6.56%)	5 / 117 (4.27%)
occurrences (all)	1	6	7
Herpes zoster			
subjects affected / exposed	3 / 56 (5.36%)	1 / 61 (1.64%)	4 / 117 (3.42%)
occurrences (all)	3	1	4
Respiratory tract infection			
subjects affected / exposed	4 / 56 (7.14%)	0 / 61 (0.00%)	4 / 117 (3.42%)
occurrences (all)	6	0	6
Pharyngitis			
subjects affected / exposed	3 / 56 (5.36%)	0 / 61 (0.00%)	3 / 117 (2.56%)
occurrences (all)	4	0	4
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	3 / 56 (5.36%)	2 / 61 (3.28%)	5 / 117 (4.27%)
occurrences (all)	3	2	5
Dehydration			
subjects affected / exposed	3 / 56 (5.36%)	1 / 61 (1.64%)	4 / 117 (3.42%)
occurrences (all)	3	1	4

Notes:

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Adverse event affected female participants only.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 June 2015	Protocol Amendment 1 (Global) included the following significant changes from the original protocol: • An allowance for interim analyses was added to the protocol to provide long-term safety and efficacy data for this ongoing study. • Exclusion criteria for unresolved meningococcal infection and for hypersensitivity to murine proteins or to one of the excipients in eculizumab were added to protect participant safety.
19 December 2016	Protocol Amendment 2 (Global) included the following significant changes from the original protocol: • The addition of a post-treatment follow-up to allow the Sponsor to collect information concerning MG status in participants post-treatment up to 1 year from the end-of-study/early termination visit. • The addition of Appendix 11 to the protocol to provide further details regarding the post-treatment information collection, including: 1. Study participants will be provided an updated informed consent form (ICF) (and/or ICF Addendum) for consent to post-treatment information collection by the Sponsor. 2. Summarizing the reason for collecting follow-up information, what information will be collected, the route(s) through which the information may be collected, and how the information will be used.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30767274

http://www.ncbi.nlm.nih.gov/pubmed/31115842

http://www.ncbi.nlm.nih.gov/pubmed/30905021

http://www.ncbi.nlm.nih.gov/pubmed/31698177